

**REMARKS**

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.

Applicants note that claims added in the prior amendment dated January 16, 2003, were inadvertently misidentified as claims 37-50. Since claims 37-46 were already present in the application, these claims have been renumbered as claims 47-60. It is noted that the error was detected by the Patent Office since the Official Action identifies the claims as including claims 47-60.

Claims 37-46 have been cancelled in view of the fact that they were withdrawn from consideration in this application as being directed to a non-elected invention. Applicants reserve the right to pursue these claims in a divisional application.

New dependent claims 61-68 have been added directed to preferred embodiments of the invention. These claims recite that the arachidonic acid-containing oil has a 24,25-methylenecholest-5-en-3 $\beta$ -ol compositional ratio in a proportion of 0.9 or less or 0.6 or less with respect to the desmosterol compositional ratio. Claims dependent from claims 14 and 52 further specify that the oil has a 24,25-methylenecholest-5-en-3 $\beta$ -ol compositional ratio of 33% or lower or 30% or lower. Support for these claims may be found at the very least at page 10, lines 9-15. No new matter has been added in these claims.

Claims 13, 14, 29, 30, 32-36 and 47-60 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Shinmen et al in view of both Shimizu et al and Barclay. This rejection is respectfully traversed.

Shinmen is said to teach that an unsaturated fatty acid-containing oil contains about 18-60% arachidonic acid. Shimizu et al is also said to teach that unsaturated fatty acid-containing oil obtained from culturing microorganism *Mortierella* has 24,25-methylenecholest-5-en-3 $\beta$ -ol, which has not been found in nature, but does not teach how much is present in the oil. Barclay is cited as teaching the employment of arachidonic acid containing oil for food products, such as baby and animal food. It allegedly would have been obvious to modify the unsaturated fatty acid-containing oil of Shinmen et al by removing the biologically unknown compound, i.e., 24,25-methylenecholest-5-en-3 $\beta$ -ol, and to employ the modified oil in food products, e.g., baby food, animal food or nutritive dietary supplement, since the biological activity was not known.

It is respectfully submitted that the instantly claimed invention would not be obvious in view of the cited art. The cited art would not be combined as proposed in the Official Action, absent the impermissible use of hindsight reconstruction, to obtain the claimed invention. Barclay, cited in the Official Action, shows that the invention as claimed was not obvious, as alleged. Barclay was filed in January of 1995, well after the publication of Shinmen in 1989 and Shimizu et al in 1992. While Barclay mentions that "it is preferable that arachidonic acid containing oil produced for use with infant formula contain little or no other long chain highly unsaturated fatty acids (e.g., eicosapentanoic acid)," Barclay makes no mention of the presence of, or testing for, the presence of 24,25-methylenecholest-5-en-3 $\beta$ -ol. Since the arachidonic acid in Barclay is produced using a *Mortierella* microorganism, if it would have been obvious in view of the teachings of Shinmen and

Shimizu, to look for the presence of 24,25-methylenecholest-5-en-3 $\beta$ -ol and remove the 24,25-methylenecholest-5-en-3 $\beta$ -ol prior from arachidonic acid containing oils to use the oils in food products, then Barclay should have at least disclosed testing the arachidonic acid containing oil for the presence of 24,25-methylenecholest-5-en-3 $\beta$ -ol and that any amount present should be removed. Since Barclay was well after Shimizu and Shinmen, at the very least, there should have been some teaching regarding the compound's presence and/or removal, if it was obvious as alleged in the Official Action.

Moreover, the Official Action alleges that "it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to modify the unsaturated fatty acid-containing oil of Shinmen et al. by *removing* the biologically unknown compound, i.e., 24,25-methylenecholest-5-en-3 $\beta$ -ol and employ the modified oil in food products such as baby food and animal food or in nutritive dietary supplement." Page 3. However, there is nothing cited regarding how one skilled in the art would accomplish the removal of the 24,25-methylenecholest-5-en-3 $\beta$ -ol. There is nothing in any of the cited references teaching how the substance would be removed from the oil.

It is respectfully submitted that it would not have been obvious, at the time of the invention, to remove the 24,25-methylenecholest-5-en-3 $\beta$ -ol from the arachidonic acid-containing oil such that a ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol is 1.2 or less, 0.9 or less or 0.6 or less, as recited in the claims. It would not have been known

that the 24,25-methylenecholest-5-en-3 $\beta$ -ol could be removed to obtain such a low ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol.

Submitted herewith is a Declaration Under 37 C.F.R. §1.132. In the Declaration, arachidonic acid is produced in accordance with the teachings of Shimizu et al (Experiment No. 1) and Shinmen et al (Experiment No. 2). As shown in the Declaration, the methods of Shimizu and Shinmen, when conducted in a fermentor, will not produce an arachidonic acid-containing oil as recited in the claims. The ratios of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol obtained are significantly higher than the claimed ratios of 1.2 or less, 0.9 or less, and 0.6 or less. *See*, Paragraphs 5, 8 and 9 of the Higashiyama Declaration. As explained in the Declaration, the prior art arachidonic acid-containing oils, when produced in a fermentor as claimed, had significantly higher ratios of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol. It would not have been obvious that an arachidonic acid-containing oil produced in a fermentor as claimed would have such a low ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol, as recited in the claims.

There is no mention in Shimizu et al or Shinmen or Barclay that a low concentration of 24,25-methylenecholest-5-en-3 $\beta$ -ol, i.e., in a ratio of 1.2 or less with respect to desmosterol, could be obtained. As shown in the enclosed Declaration, the strain of Shimizu et al does not produce 24,25-methylenecholest-5-en-3 $\beta$ -ol in the claimed ratio. As shown in Experiment 1, for example, when produced in a fermentor, the ratio was significantly higher than that obtained by the instant invention. Similarly, Experiment 2 shows that the strain disclosed in Shinmen et al does not produce 24,25-

methylenecholest-5-en-3 $\beta$ -ol in the claimed ratio. Thus, there is nothing cited in the rejection which would teach or even suggest that an arachidonic acid-containing oil as claimed, having such a low ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol, would even be possible.

Nor is there any teaching in the cited art to remove 24,25-methylenecholest-5-en-3 $\beta$ -ol to obtain the claimed oil having the specified ratio. Elimination of 24,25-methylenecholest-5-en-3 $\beta$ -ol present in a fatty acid-containing product is very difficult. The difficulty is due to the fact that the polarity of the 24,25-methylenecholest-5-en-3 $\beta$ -ol and of oil contained in a fermentation broth are substantially the same. Therefore, conventional purification methods cannot be used to simply remove the 24,25-methylenecholest-5-en-3 $\beta$ -ol from the oil. Applicants are not aware of *any* references describing a method for removing the 24,25-methylenecholest-5-en-3 $\beta$ -ol from oil or lipid.

In the instant specification, Examples 1-3 describe the ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol in a hexane extract, and Example 4 describes the same ratio in oil after purification. First, it should be noted that substantially all the lipid components are extracted by hexane; therefore, the ratio in lipid in a fermentation broth before the extraction and the ratio in the hexane extract are substantially the same.

According to Example 1, the 24,25-methylenecholest-5-en-3 $\beta$ -ol content is 30% and the desmosterol content is 66% to give a ratio of 0.46. According to Example 2, the 24,25-methylenecholest-5-en-3 $\beta$ -ol is 25% and the desmosterol content is 53%, to give a ratio of 0.47. According to Example 3, the 24,25-methylenecholest-5-en-3 $\beta$ -ol content is

5% and the desmosterol content is 67% or 35%, to give a ratio of 0.07 or 0.14, respectively. In Example 4, the 24,25-methylenecholest-5-en-3 $\beta$ -ol content is 24% and the desmosterol content is 67%, to give a ratio of 0.35.

It is clear that a conventional purification process as described in Example 4 cannot change the ratio of the 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol content. Thus, to obtain a final lipid or oil product having the ratio of 24,25-methylenecholest-5-en-3 $\beta$ -ol to desmosterol content within the claimed ratio, it is essential to obtain a crude lipid or oil in a fermentation broth in which the ratio in that crude lipid or oil is within the claimed ratio. How to obtain such a lipid or oil is nowhere taught or suggested in the cited references. Without a means in the art for obtaining the oil as claimed, the product itself cannot have been known or obvious prior to Applicant's invention.

Thus, even by combining the references as proposed in the Official Action, the claimed invention is still not obtained. Withdrawal of the prior art rejection of record is respectfully requested. Such action is believed to be in order.

In view of the above, it is respectfully submitted that the claimed invention is not disclosed by, nor rendered obvious by the cited art. Withdrawal of the rejection of record is respectfully submitted and believed to be in order.

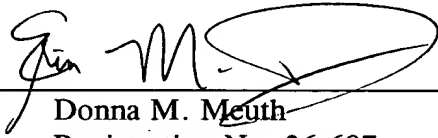
It is respectfully submitted that the application is now in condition for allowance. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (650) 622-2360 so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: August 11, 2003

By:  #51,147  
for Donna M. Meuth  
Registration No. 36,607

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620